



Patient Blood Management in orthopaedic surgery: a four-year follow-up of transfusion requirements and blood loss from 2008 to 2011 at the Balgrist University Hospital in Zurich, Switzerland

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Abstract: **BACKGROUND:** The aim of this study was to investigate the impact of the introduction of a Patient Blood Management (PBM) programme in elective orthopaedic surgery on immediate pre-operative anaemia, red blood cell (RBC) mass loss, and transfusion. **MATERIALS AND METHODS:** Orthopaedic operations (hip, n=3,062; knee, n=2,953; and spine, n=2,856) performed between 2008 and 2011 were analysed. Period 1 (2008), was before the introduction of the PBM programme and period 2 (2009 to 2011) the time after its introduction. Immediate pre-operative anaemia, RBC mass loss, and transfusion rates in the two periods were compared. **RESULTS:** In hip surgery, the percentage of patients with immediate pre-operative anaemia decreased from 17.6% to 12.9% ($p<0.001$) and RBC mass loss was unchanged, being 626 ± 434 vs 635 ± 450 mL ($p=0.974$). Transfusion rate was significantly reduced from 21.8% to 15.7% ($p<0.001$). The number of RBC units transfused remained unchanged ($p=0.761$). In knee surgery the prevalence of immediate pre-operative anaemia decreased from 15.5% to 7.8% ($p<0.001$) and RBC mass loss reduced from 573 ± 355 to 476 ± 365 mL ($p<0.001$). The transfusion rate dropped from 19.3% to 4.9% ($p<0.001$). RBC transfusions decreased from 0.53 ± 1.27 to 0.16 ± 0.90 units ($p<0.001$). In spine surgery the prevalence of immediate pre-operative anaemia remained unchanged ($p=0.113$), RBC mass loss dropped from 551 ± 421 to 404 ± 337 mL ($p<0.001$), the transfusion rate was reduced from 18.6 to 8.6% ($p<0.001$) and RBC transfusions decreased from 0.66 ± 1.80 to 0.22 ± 0.89 units ($p=0.008$). **DISCUSSION:** Detection and treatment of pre-operative anaemia, meticulous surgical technique, optimal surgical blood-saving techniques, and standardised transfusion triggers in the context of PBM programme resulted in a lower incidence of immediate pre-operative anaemia, reduction in RBC mass loss, and a lower transfusion rate.

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Patient blood management in orthopaedic surgery: a four-year follow-up of transfusion requirements and blood loss from 2008 to 2011 at the Balgrist University Hospital in Zurich, Switzerland

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Background. The aim of this study was to investigate the impact of the introduction of a Patient Blood Management (PBM) programme in elective orthopaedic surgery on immediate pre-operative anaemia, red blood cell (RBC) mass loss, and transfusion.

Materials and methods. Orthopaedic operations (hip, n=3,062; knee, n=2,953; and spine, n=2,856) performed between 2008 and 2011 were analysed. Period 1 (2008), was before the introduction of the PBM programme and period 2 (2009 to 2011) the time after its introduction. Immediate pre-operative anaemia, RBC mass loss, and transfusion rates in the two periods were compared.

Results. In hip surgery, the percentage of patients with immediate pre-operative anaemia decreased from 17.6% to 12.9% (p<0.001) and RBC mass loss was unchanged, being 626±434 vs 635±450 mL (p=0.974). Transfusion rate was significantly reduced from 21.8% to 15.7% (p<0.001). The number of RBC units transfused remained unchanged (p=0.761). In knee surgery the prevalence of immediate pre-operative anaemia decreased from 15.5% to 7.8% (p<0.001) and RBC mass loss reduced from 573±355 to 476±365 mL (p<0.001). The transfusion rate dropped from 19.3% to 4.9% (p<0.001). RBC transfusions decreased from 0.53±1.27 to 0.16±0.90 units (p<0.001). In spine surgery the prevalence of immediate pre-operative anaemia remained unchanged (p=0.113), RBC mass loss dropped from 551±421 to 404±337 mL (p<0.001), the transfusion rate was reduced from 18.6 to 8.6% (p<0.001) and RBC transfusions decreased from 0.66±1.80 to 0.22±0.89 units (p=0.008).

Discussion. Detection and treatment of pre-operative anaemia, meticulous surgical technique, optimal surgical blood-saving techniques, and standardised transfusion triggers in the context of PBM programme resulted in a lower incidence of immediate pre-operative anaemia, reduction in RBC mass loss, and a lower transfusion rate.

Keywords: anaesthesia audit, pre-anaesthetic assessment, blood transfusion, orthopaedic surgery.

Introduction

Despite risks, red blood cell (RBC) transfusions remain common practice in elective orthopaedic surgery^{1,2}. In addition to transfusion risks, such as, transmission of bacterial or viral infections, febrile transfusion reactions, transfusion-related acute lung injury, a relationship of causality has recently been shown between allogeneic RBC transfusions and increased mortality, morbidity and immunomodulation³. When considering the burden of cost on public health systems, RBC transfusions become a relevant issue⁴. The approximate cost of administering one unit of RBC is US\$ 700-1,200 and treating the associated side effects may cost \$1,000^{5,6}.

In orthopaedic surgery, the prevalence of pre-operative anaemia varies from 20% to 51%⁷⁻⁹ and is defined by the World Health Organisation (WHO) as a haemoglobin level

≤12 g/dL in women and ≤13 g/dL in men, corresponding to a haematocrit of ≤36% in woman and ≤39% in men. Pre-operative anaemia is an independent risk factor for increased 30-day mortality and major morbidity in all surgical patients¹⁰⁻¹². In up to 30% of patients, iron deficiency is the cause of anaemia and should be corrected at least 4 weeks prior to surgery to achieve optimal results^{1,9}. Optimising haemoglobin mass before orthopaedic surgery as well as limiting intra-operative blood loss is associated with improved outcomes after 90 days¹³.

The WHO urges member states to utilise transfusion alternatives and develop individualised Patient Blood Management (PBM) programmes reducing transfusion needs. The three pillars of PBM are: (i) detection and treatment of pre-operative anaemia, (ii) reduction in peri-operative RBC loss, and (iii) harnessing and optimising the patient-specific physiological reserve of

anaemia (including restrictive haemoglobin transfusion triggers)¹⁴⁻¹⁷.

The aim of this study was to investigate the effects of implementing a PBM programme on: (i) immediate pre-operative anaemia, (ii) intra-operative RBC mass loss as well as blood volume loss, and (iii) transfusion rates.

Material and methods

Data collection was started after obtaining approval from the local ethics committee (Kantonale Ethikkommission Zurich, Switzerland, study number KEK-ZH-Nr. 2010-0263/4).

The PBM programme was initiated in 2009 at the Department of Orthopaedics, University of Zurich, Balgrist Hospital, Zurich, Switzerland. Data from 2008 were analysed retrospectively and were considered the baseline with regards to the prevalence of immediate pre-operative anaemia, intra-operative RBC mass loss and blood volume loss, and overall transfusion rate of RBC, platelet concentrates and fresh-frozen plasma (period 1). The span from 2009 to 2011 was analysed prospectively and was considered the time after the introduction of PBM (period 2).

The PBM programme at the Department of Orthopaedics in Balgrist Hospital had the following components: (i) investigation for pre-operative anaemia and treatment, (ii) reduction of intra-operative blood loss by surgical, anaesthesiological and pharmacological techniques, and (iii) lowering of the transfusion trigger to a haemoglobin level of ≤ 8 g/dL; a reduction of 2 g/dL compared to 2008^{14,15}.

In the PBM programme all patients undergoing elective orthopaedic surgery (hip, knee and spine interventions) had to be reported (name of the patient, type of surgery, date of surgery) approximately 4 weeks prior to surgery to a designated anaesthesiologist of the Institute of Anaesthesiology at the University Hospital Zurich, Zurich, Switzerland. If reported the patient's general practitioner was contacted to get the latest haemoglobin concentration as well as C-reactive protein level.

Criteria for treating anaemic patients with intravenous iron and erythropoietin were that the patient was older than 18 years, scheduled to undergo major orthopaedic surgery (hip or knee arthroplasty or back surgery including scoliosis, laminectomy, decompression and disc hernia), had a haemoglobin <13.0 g/dL if male or <12.0 g/dL if female, and that it was 4 ± 1 weeks prior to surgery. Criteria for not treating anaemic patients with intravenous iron and erythropoietin were that the patient had active severe infection/inflammation (defined as serum C-reactive protein >20 mg/L), diagnosed malignancy, known history of hepatitis B/C or positivity for human immunodeficiency virus, was

receiving immunosuppressive or myelosuppressive therapy, had a concurrent medical condition(s) that, in the view of the investigator, would prevent compliance or participation or jeopardise the patient's health, was pregnant or breastfeeding, had a history of thromboembolic events, severe peripheral, coronary or carotid artery disease, weighed <50 kg, and was not able to understand the German language. Furthermore data were not collected for operations performed on minors (defined as individuals under 18 years of age) or any revisions within 8 weeks of the initial surgery.

In cases of anaemia a recommended therapy was administered consisting of 1,000 mg of iron carboxymaltose (Ferinject®, Vifor International AG, St. Gallen, Switzerland, price Swiss Fr 254.80) intravenously over 15 minutes, 40,000 IU of erythropoietin alpha subcutaneously (Eprex®, Janssen-Cilag AG, Baar, Zug, Switzerland, price Swiss Fr 481.80), 1 mg vitamin B12 subcutaneously (Betolvex®, Actavis Switzerland AG, Regensdorf, Switzerland, price Swiss Fr 1.85) and 5 mg folic acid (AcidumfolicumStreuli®, StreuliPharma AG, Uznach, Switzerland, price Swiss Fr 0.70) orally per day for 4 weeks. Laboratory controls after 14 days were advised. In cases of persisting anaemia a second dose of iron carboxymaltose, erythropoietin, and vitamin B12 was administered. To reduce intra-operative blood loss, cell salvage, topical haemostatic agents, and meticulous intra-operative haemostasis were used¹⁸. Tranexamic acid and post-operative cell salvage were not used during the study period.

Data collection

Data from database of the Department of Orthopaedics, Balgrist Hospital for all hip, knee, and spine operations performed between 2008 and 2011 were matched with those from the laboratory and transfusion databases of the Central Laboratory of Zurich (Zurich, Switzerland) using the patient's name, case number and date of birth as a unique identifier. All data were transferred into an Excel-chart (Microsoft® Office 2010, Microsoft® Corporation, Redmond, WA, USA). Demographic data including date of birth, sex, weight and height, age at the date of surgery, as well as surgery-specific details were collected. Pre-operative haemoglobin and haematocrit values, up to 21 days before surgery, as well as haemoglobin and haematocrit values for post-operative days 1 to 5, were collected. The total number of RBC units, platelet concentrates, and fresh-frozen plasma units transfused during the first 5 days after surgery were recorded. Haemoglobin values of the preoperative day were available for all patients and the prevalence of anaemia was determined. Missing post-operative Haemoglobin and haematocrit values led to the patient being excluded from RBC mass loss and

blood loss analysis. Pre-operative data were available for 3,062 cases of hip surgery, 2,953 cases of knee surgery, and 2,856 spine operations. Complete post-operative data were available for 1,842, 984 and 1,432 hip, knee and spine operations, respectively.

The formulae used to calculate peri-operative RBC mass loss and blood volume loss are shown in Table I. Two formulae were initially used for total blood volume loss: one factoring in the mean haematocrit and the other the formula of Brecher^{19,20}.

Statistical analysis

Continuous variables are presented as means with standard deviations or medians with ranges, categorical variables are presented as numbers with proportions. Data from 2009 to 2011 were combined (period 2) and compared to those from 2008 (period 1) using the Mann-Whitney test and the chi-square test when appropriate. No adjustment for multiple comparisons was performed in this analysis. The IBM SPSS Statistics version 20 statistical programme (SPSS Inc., Chicago, IL, USA) was used for statistical analyses. Two-sided p values less than 0.05 were considered statistically significant.

Results

Demographic data and reporting

The demographic data (Table II) show that patients undergoing elective hip surgery ($p=0.001$) and knee surgery ($p<0.001$) were significantly younger in period 2 than in period 1 ($p=0.001$ for hip surgery, $p<0.001$ for knee surgery). Patients undergoing elective orthopaedic interventions (hip, knee, and spine surgery) were reported 35 ± 11 days prior to surgery to a designated anaesthesiologist of the Institute of Anaesthesiology at the University Hospital Zurich, Switzerland.

Effect of the implementation of Patient Blood Management on immediate pre-operative anaemia

The prevalence of immediate pre-operative anaemia decreased significantly from period 1 to period 2 in hip and knee surgery, from 17.6 % to 12.9 % ($p<0.001$) and 15.5% to 7.8% ($p<0.001$), respectively. In spine surgery immediate pre-operative anaemia stayed the same (12.6% vs 10.3%; $p=0.113$). Overall 9% of the reported patients were treated for anaemia with one dose of intravenous iron and erythropoietin. Only 15% of these patients needed a second treatment. On the day of surgery none of these patients was anaemic anymore.

Table I - Formulae used to calculate data^{19,20}.

Data calculated	Formula used
Total RBC mass loss	Uncompensated loss+compensated loss
Compensated RBC mass loss	$275 \text{ mL} \times 0.6 \times \text{RBC Units transfused}$
Uncompensated RBC mass loss	Initial RBC Volume-Finale RBC Volume
Initial RBC mass	$(\text{Hct Pre-op}/100) \times \text{BV}$
Finale RBC mass	$(\text{Hct lowest D1 to D5}/100) \times \text{BV}$
Body surface	$0.0235 \times (\text{height}^2 \times 0.42246) \times (\text{weight}^2 \times 0.51456)$
Estimated blood volume	Woman: $\text{Body Surface} \times 2,430$ Man: $\text{Body Surface} \times 2,530$
Blood volume loss mean formula	$\text{Total loss} / ((\text{Hct pre-OP} + \text{MIN}(\text{Hct1}; \text{Hct2}; \text{Hct3}; \text{Hct4}; \text{Hct5}))) / 200$
Blood volume loss Brecher formula	$\text{EBV} \times \text{LN}(\text{Hct pre-OP} / \text{MIN}(\text{Hct1}; \text{Hct2}; \text{Hct3}; \text{Hct4}; \text{Hct5}))$

Blood volume loss was calculated using both the Brecher formula and the formula using a mean Hct out of the preoperative and lowest post-operative values.

Table II - Demographic data of patients undergoing elective hip, knee, or spine surgery according to periods.

	Hip			Knee			Spine		
	period 1	period 2	p	period 1	period 2	p	period 1	period 2	p
Males, %	43.70	47.40	0.201	38.50*	46.80*	0.034*	43.00	47.00	0.369
Females, %	56.30	52.60	0.202	61.50*	53.20*	0.028*	57.00	53.00	0.429
Age	64±14*	59±17*	<0.001*	67±12*	61±16*	<0.001*	60±15	62±15	0.893
Body mass index	26.5±5.0	26.5±5.2	0.698	30.0±6.9	28.9±5.6	0.052	26.5±4.5	26.7±5.5	0.467
N. of patients pre-op	797	2,265		710	2,243		643	2,213	
N of patients post-op	387	1,455		187	797		107	1,317	

Data shown are mean±SD. Period 1 shows data from the year 2008 (before the introduction of the PBM programme), period 2 refers to the years 2009-2011 (after the introduction of the PBM program). *: significant difference between the periods. N of patients pre-op: number of patients with complete data pre-operatively; N. of patients post-op: number of patients with complete data post-operatively.

The mean increase of haemoglobin was 2.00 ± 0.48 g/dL from one dose of treatment. The peri-operative evolution of haemoglobin in period 1 and 2 is shown in Figure 1.

Effect of the implementation of Patient Blood Management on loss of red blood cell mass and blood volume

The RBC mass loss was calculated using the formulae in Table I and results are presented in Figure 2 (A-C) by type of surgery. To transform the RBC mass loss into blood volume loss, two formulae were used and compared: one accounting for the mean haematocrit between the pre-operative value and the lowest

post-operative value, the other being the formula of Brecher (Table I)¹⁹. There was no significant difference between these two methods in terms of calculated blood volume loss. The results of the two formulae regarding blood volume loss are presented in Figure 2 (A-C). The formulae showed identical results: the mean formula is, therefore, used to compare the two periods.

For hip surgery, RBC mass loss as well as blood volume loss remained unchanged when comparing period 1 vs period 2 [RBC mass 626 ± 434 mL vs 635 ± 450 mL ($p=0.974$); blood loss $1,402 \pm 728$ mL vs $1,453 \pm 761$ mL ($p=0.462$)]. In knee surgery, RBC mass loss and blood volume loss decreased significantly

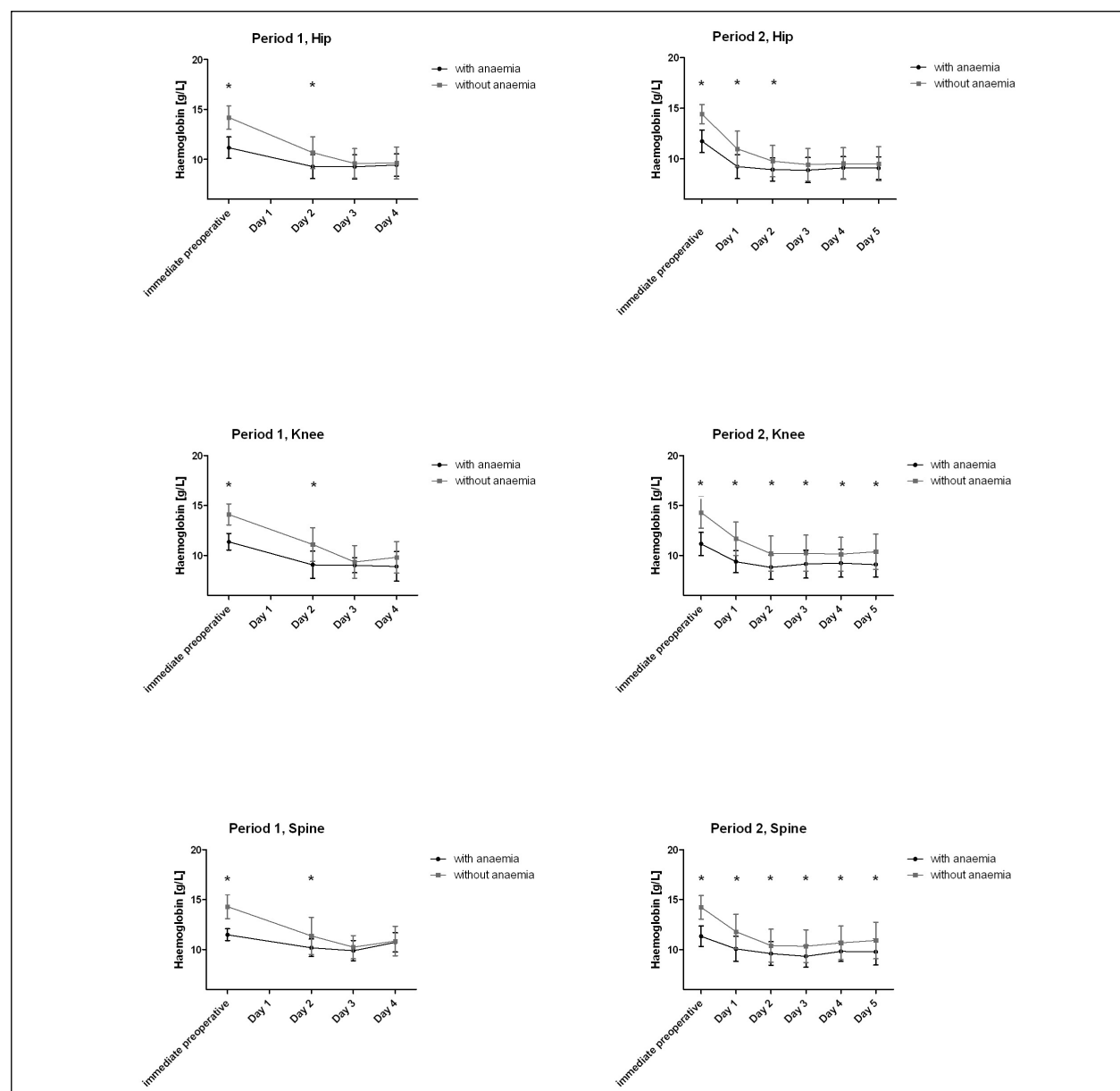


Figure 1 - Evolution of haemoglobin in non-anaemic and immediate preoperative anaemic patients by type of surgery and period. *: $p < 0.05$ for anaemic vs non anaemic patients.

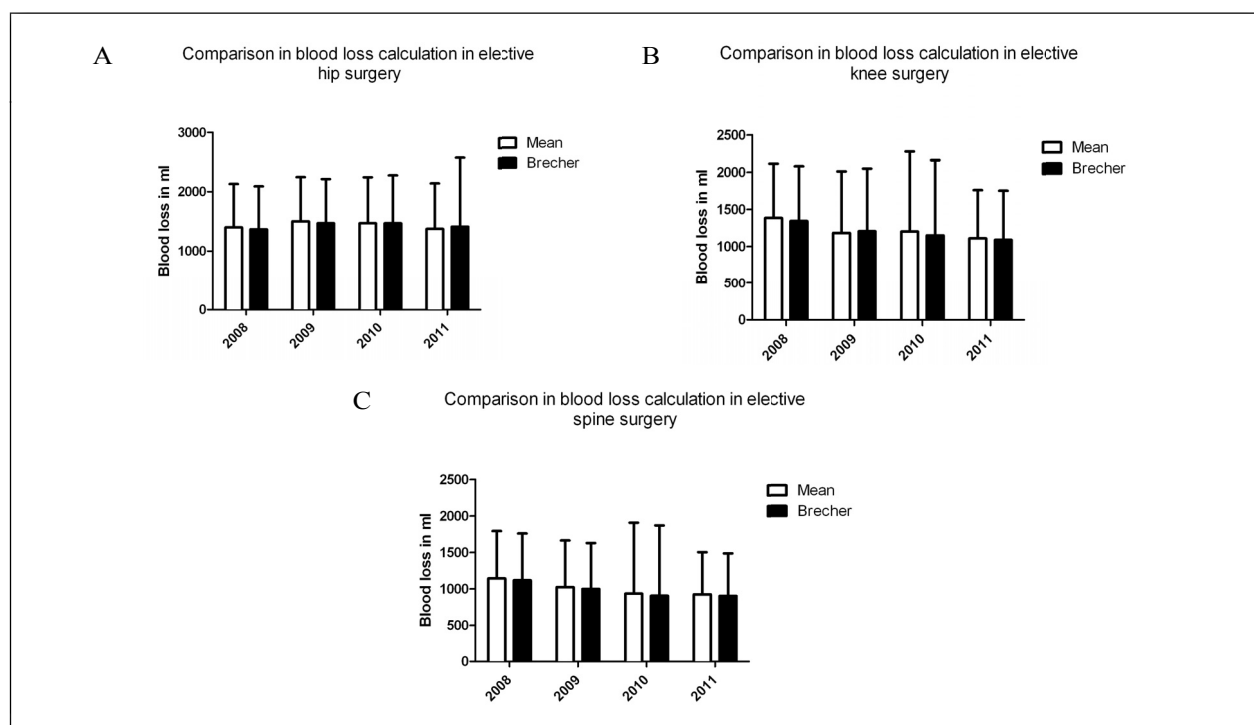


Figure 2 - Comparison between blood volume loss calculations according to the mean formula and the Brecher formula. A: elective hip surgery, B: elective knee surgery, C: elective spine surgery.

Formulae used: Blood volume loss according to the mean formula: $\text{Total loss}/[(\text{Hct pre-OP} + \text{MIN}(\text{Hct1}; \text{Hct2}; \text{Hct3}; \text{Hct4}; \text{Hct5}))/200]$; Blood volume loss according to the Brecher Formula: $\text{EBV} \times \text{LN} (\text{Hct pre-OP}/\text{MIN}(\text{Hct1}; \text{Hct2}; \text{Hct3}; \text{Hct4}; \text{Hct5}))$.

from 573 ± 355 mL to 476 ± 365 ($p < 0.001$) and from $1,384 \pm 731$ mL to $1,164 \pm 852$ mL ($p < 0.001$) in period 1 vs period 2, respectively. In spine surgery there were also significant reductions in RBC mass loss (from 551 ± 421 mL in period 1 to 404 ± 337 mL in period 2; $p < 0.001$) and blood volume loss (from $1,143 \pm 649$ mL to 960 ± 730 mL; $p = 0.005$).

Effect of the implementation of Patient Blood Management on transfusion rates

Transfusion rates of anaemic patients were consistently higher than in non-anaemic patients ($p < 0.001$) in all three types of surgery and each year (Table III).

In hip surgery overall transfusion rates decreased significantly from 21.8% to 15.7% ($p < 0.001$). A mean of 0.82 ± 1.94 units of RBC was transfused in period 1 compared to 0.62 ± 1.96 units in period 2 ($p = 0.761$). A mean of 0.12 ± 0.73 units of fresh-frozen plasma was transfused in period 1 compared to 0.08 ± 0.63 units in period 2 ($p = 0.601$). Platelet transfusions remained unchanged at 0.01 ± 0.71 in period 1 and 0.00 ± 0.09 units in period 2 ($p = 0.591$).

The overall transfusion rates decreased significantly ($p < 0.001$) in knee surgery (from 19.3% to 4.9%). A mean of 0.53 ± 1.27 units of RBC was transfused in period 1 compared to 0.16 ± 0.90 in

period 2 which represented a significant reduction ($p < 0.001$). Platelet transfusions remained unchanged (from 0.00 ± 0.00 to 0.00 ± 0.03 units; $p = 0.574$) as did fresh-frozen plasma transfusions (from 0.02 ± 0.25 to 0.01 ± 0.22 units; $p = 0.388$) in period 1 and period 2, respectively.

Table III - Transfusion of patients anaemic or non-anaemic immediately pre-operatively.

Year	Surgery	Transfusion in non-anaemic patients (%)	Transfusion in anaemic patients (%)	p
2008	Hip	14.7	60.0	<0.0001
2009	Hip	10.2	38.5	<0.0001
2010	Hip	14.9	49.7	<0.0001
2011	Hip	15.5	39.9	<0.0001
2008	Knee	13.3	53.6	<0.0001
2009	Knee	8.4	40.8	<0.0001
2010	Knee	6.2	28.9	<0.0001
2011	Knee	5.5	37.3	<0.0001
2008	Spine	13.8	53.8	<0.0001
2009	Spine	9.8	40.6	<0.0001
2010	Spine	10.9	39.7	<0.0001
2011	Spine	6.8	25.6	<0.0001

For spine surgery the overall transfusion rates decreased significantly ($p<0.001$) from 18.7% to 8.6%. A mean of 0.66 ± 1.80 units of RBC was transfused in period 1 compared to 0.22 ± 0.89 units in period 2 ($p=0.008$). Platelet transfusions decreased significantly from 0.01 ± 0.09 in period 1 to 0.00 ± 0.00 units in period 2 ($p<0.001$) and fresh-frozen plasma transfusions decreased significantly from 0.11 ± 0.46 units in period 1 to 0.03 ± 0.30 units ($p<0.001$) in period 2.

Discussion

The introduction of a multidisciplinary PBM programme in elective orthopaedic surgery reduced the prevalence of immediate pre-operative anaemia, reduced RBC mass loss as well as the blood volume loss, and reduced the need for blood transfusions. This 4-year investigation shows that immediate pre-operative anaemia, RBC mass loss as well as blood volume loss, and transfusion rates can be reduced by creating awareness, using preventive measures and changing culture. The PBM introduced at the Department of Orthopaedics in Balgrist Hospital is in accordance with the WHO 2010 recommendations²¹ and confirms the results of a systematic review on the efficacy of PBM measures²².

Contacting the patients' general practitioners at least 4 weeks prior to surgery in order to pick up and treat anaemia was key in lowering the incidence of immediate pre-operative anaemia. A foreseeable obstacle to treating anaemia pre-operatively is that patients' operations are scheduled within less than 4 weeks which leaves little time to correct anaemia. Awareness among orthopaedic surgeons and general practitioners regarding pre-operative anaemia needs to be increased in order that there is sufficient time to treat the anaemia prior to surgery, although there is only one report indicating that even short-term treatment with intravenous iron and an erythropoiesis-stimulating agent may decrease transfusion needs in surgery²³. In accordance with the findings of Rosencher *et al.* in 2005 one to two doses of erythropoietin are sufficient to increase haemoglobin to non-anaemic levels²⁴.

In an Austrian benchmark study, Gombotz *et al.* showed that up to now 90% of cases of pre-operative anaemia are not treated prior to elective surgery with expected significant blood loss resulting in a 3- to 4-fold increase in transfusion rates¹. In 2008, the Department of Orthopaedics in Balgrist Hospital started with a relatively low immediate pre-operative anaemia rate of 18%, which was higher than the 7.3% observed by Enko *et al.* in 370 orthopaedic patients²⁴ but lower than the 22.4% found by Seicean *et al.* in 24,473 spinal operations^{25,26}.

In 2003, Rosencher *et al.* reported a blood volume loss of $2,143\pm1,165$ mL in primary hip surgery and $2,072\pm1,145$ mL in primary knee surgery⁸. Our current

data on blood volume loss are lower in hip surgery ($1,453\pm761$ mL) and knee surgery ($1,164\pm852$ mL). Oberhofer *et al.* reported similar results to ours with a total blood volume loss of $1,330\pm635$ mL in total hip surgery and of $1,427\pm660$ mL in total knee replacement surgery²⁷.

In spine surgery (including scoliosis and cancer surgery) blood volume loss decreased to 923 ± 580 mL. This is remarkably low when compared to the data in the meta-analysis by Chen *et al.*, who reported a blood volume loss of 2,180 mL (95% CI: 1,805-2,554 mL)²⁸. The differences in blood loss may be explained by factoring in surgical experience and techniques which could contribute to our findings of smaller volumes of blood lost. Tranexamic acid can reduce blood volume loss further, as described in several publications, although it was not used in the Department of Orthopaedics in Balgrist Hospital^{29,30}.

We observed a significant reduction in administered blood products in relation to the surgeons accepting a reduction in the transfusion trigger from 10 g/dL to 8 g/dL and the reduction in intra-operative blood volume loss. The transfusion rates varied depending on the type of surgery from 15.7% in hip surgery to 4.9% in knee surgery; these percentages are lower than those reported by Qian *et al.*, who analysed 54,405 total hip replacement operations in which the overall RBC transfusion rate was 31%³¹.

The use of intravenous *vs* oral iron is presently being discussed. In 2007, Theusinger *et al.* showed that the use of intravenous iron sucrose was efficacious and safe⁹. A recent study by Munoz *et al.* also showed the safety and efficacy of intravenous iron administration³². One of the advantages of intravenous iron is that it is more effective; furthermore, compliance is higher with intravenous iron than with oral iron. The European Society of Anaesthesiology recently recommended intravenous and oral iron with a 1B grading each, with some restrictions using intravenous iron only if oral iron is contraindicated³³. The recently published meta-analysis by Litton *et al.* on intravenous *vs* oral iron needs to be interpreted cautiously with regard to the peri-operative period³⁴ since only 11 of the 72 studies considered were performed in the context of surgery and in only 10 of the 72 studies was ferric carboxymaltose. Furthermore no increase in infections was observed with intravenous iron in patients after surgery, and the combination of intravenous iron and erythropoietin has been found to be the most efficient therapy for anaemia. Interestingly, Munoz *et al.* recently described a significant reduction of nosocomial infections in patients undergoing orthopaedic surgery when treated pre-operatively with intravenous iron³².

The approximate cost of administering one unit of RBC is US\$ 700-1,200 and treating the associated

side effects may cost \$ 1,000^{5,6}. The cost of the applied treatment of 40,000 IU erythropoietin alpha, 1 g of intravenous iron, vitamin B12 and folic acid was Swiss Fr 739.15 (~US\$ 815) which is still cheaper than one unit of RBC and its side effects.

This study has several limitations as 2008 was analysed retrospectively, whereas 2009 through to 2011 prospectively. Peri-operative data were available for all patients, whereas complete postoperative data were available for only 60% of hip operations, 33% of knee operations, and 50% of spinal operations. A possible explanation of this difference would be that post-operative haemoglobin levels were not measured in patients who had high pre-operative haemoglobin levels and small volumes of blood loss intra-operatively. The length of stay could not be analysed since the duration of hospitalisation was very strongly influenced by a variety of contracts between the Department of Orthopaedics, Balgrist Hospital and a number of health insurance companies. In addition, these contracts varied over time during the study period, leading to a standardised length of stay for all patients who underwent certain surgical interventions.

The pre-operative iron status was not assessed systematically. We adapted the anaemia treatment to the local situation. Over the years we tried to make the orthopaedic surgeons assess their patients' haemoglobin level and iron status approximately 4 weeks pre-operatively, which turned out not to be successful. In order to get a PBM programme running, the orthopaedic surgeons agreed to inform a designated anaesthesiologist on each patient they scheduled for surgery. The anaesthesiologist then contacted the patient's general physician who knew the patient's haemoglobin although only relatively few general physicians assessed their patients' iron status. Since we wanted the anaemic patients to be treated we opted for a pragmatic treatment including intravenous iron, erythropoietin alpha, vitamin B12 and folic acid. We are aware of the fact that this approach may appear somewhat simplistic but in the local situation it was the only way in which we could in fact have the anaemic patients treated. Now that we have shown to everybody that a PBM programme is successful, a second approach will be taken, trying to diagnose the patients in more detail and allowing a more specific treatment for the anaemia or iron deficiency.

Complications and serious adverse events could not be analysed due to changes in codification with the introduction of the Swiss DRG system and due to the fact that in 2008 no data on complications were electronically available. In addition, due to the International Classification of Diseases (ICD10) codification, it was not possible to distinguish whether the problem was a new diagnosis that developed during the current hospitalisation or whether it was present

pre-operatively. The still relatively high proportion of anaemic patients is most probably due to a lack of reporting (some patients were simply not reported to us anaesthesiologists) or reporting too late (only few days before surgery) or patients having exclusion criteria (mainly language, high C-reactive protein level, known malignancy).

In conclusion, this study shows that the implementation of a PBM programme for elective hip, knee, and spine surgery leads to a significant reduction of immediate pre-operative anaemia, intra-operative RBC mass loss as well as the blood volume loss, and transfusion needs. Further studies are needed to show long-term effects of such programmes as well as possible reductions in post-operative complications, time spent in hospital, and costs.

Funding and approval

This study was supported by departmental funds and by a grant from the Gesundheitsdirektion des Kantons Zürichs for Highly Specialized Medicine.

It was approved by the local ethics committee (Kantonale Ethikkommission Zurich, Switzerland, study number KEK-ZH-Nr. 2010-0263/4).

Authorship contribution

Oliver M. Theusinger and Stephanie L. Kind contributed equally to this study.

Oliver M. Theusinger designed the study, conducted the study, analyzed the data and wrote the manuscript. Stephanie L. Kind helped to conduct the study, write the manuscript and edited it and contributed equally to this study as Oliver M. Theusinger. Burkhardt Seifert made the statistical analysis and helped to write the manuscript. Alain Borgeat helped to conduct the study and write the manuscript. Christian Gerber helped to conduct the study and write the manuscript. Donat R. Spahn designed the study, conducted the study, and wrote the manuscript.

Conflicts of interest disclosure

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